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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/594,983 | 06/15/2000 | William C. Olson | 57906-B/JPW/SHS | 8686 |

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| EXAMINER | |
|---|---|
| FOLEY, SHANON A | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1648 | |

DATE MAILED: 07/11/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/594,983 | OLSON ET AL. | |
| | Examiner | Art Unit | |
| | Shanon Foley | 1648 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *28 February 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *98-134* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *98-134* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *1/11/5 and Exhibit D of 2/28/5*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## DETAILED ACTION

### *Information Disclosure Statement*

The IDS submitted June 11, 2004 has been considered. There is also an IDS submitted as Exhibit D with the response filed February 28, 2005. In this IDS, applicant re-submits pending claims of abandoned applications that were not previously considered because the cases are abandoned and/or because the pending claims were not previously available to the examiner. The IDS also contains new references that have not been listed previously. Although claims in unpublished, abandoned applications do not have any bearing in the instant case since the disclosures of these cases cannot be applied under any known statute, all of the references listed in exhibit D have been considered.

### *Claim Rejections - 35 USC § 112*

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 98, 102-104 and 129-134 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Amended claim 98 recites, "the hybridoma cell line....or a fragment thereof...". While it is presumed that applicant intends to claim fragments of the antibody PA14 and not fragments of the cell line, the intention is not evident from the claim language. If fragments of the cell line are intended, it cannot be determined which fragments are being claimed. This rejection also affects claims 102-104.

Claims 129-134 are drawn to a monovalent antibody. These claims ultimately depend from amended claims 100 and 101, which now require that the antibody (or fragment thereof), bind to the same epitope as monoclonal antibody PA14 or have the CDRs derived from PA14 hybridoma. Since PA14 has bi-specificity to a combination of two epitope valencies comprising an amino acid at the Nt and an amino acid within ECL2, the monovalent antibody of claims 129-134 contradicts the required elements of claims 100 and 101 since it would only be specific for one valency. Therefore, it is unclear what applicant is intending to claim for claims 129-134.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 98 and 102-104 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

As discussed above, claim 98 encompasses fragments of the hybridoma cell line, PA14. There is no support for this concept in the original disclosure and the recitation thereof presents new matter. Applicant is required to either cancel the new matter or point to support for this concept.

***Double Patenting***

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed.

Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 98-104 and 117-122 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 99-105 of copending Application No. 2004/0228869 (submitted in the IDS of Exhibit D. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims are drawn to a monoclonal antibody, PA14, or a fragment thereof, produced from a hybridoma cell line, PA14, that binds to which binds to the N-terminus of CCR5 and the second extracellular loop of CCR5. The claims also encompass monoclonal antibodies or fragments thereof, which bind to the same epitopes as PA14. The claims also encompass antibodies that comprise specific human Ig molecules. The claims of '869 are drawn to compositions comprising indistinguishable antibodies and antibody fragments from those instantly claimed. Therefore, the composition claimed is not patentably distinct from the composition of '869.

Claims 124, 127, 128, 130, 133 and 134 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 99-105 of copending Application No. 2004/0228869 in view of Wu et al. (WO 98/18826).

The claims state that the instant antibody is a chimeric antibody or comprises a human immunoglobulin molecule selected from IgG2, IgG4 or is a monovalent antibody.

See the teachings of '869 above. The reference does not teach or suggest a chimeric antibody, the human framework of the monoclonal antibodies of IgG2, IgG4, or monovalent antibodies. However, Wu et al. teach monovalent antibodies as well as humanized forms of the antibodies, where the framework and the consensus are derived from a human immunoglobulin or multiple immunoglobulin molecules, see page 15, lines 18-21, page 72, line 31, 19, line 31 to page 21, line 32 and claims 1-7, 27-32, 47-50, 55 and 56. It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to make monoclonal antibodies of '896 for monovalent specificity to one particular epitope in the region of interest. One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of success for making such antibodies because Wu et al. teach monovalent antibodies that recognize the same or similar epitopes recognized by '869. It would also have been obvious for one of ordinary skill in the art at the time the invention was made to obtain the antibody framework from any of the human immunoglobulins to maintain the conformation of the CDR region and to render the recombinant antibodies less immunogenic once administered. Further, one of ordinary skill in the art would have been motivated to maintain the donor amino acid sequences immediately adjacent to the CDR domains to assure that when the framework portion of the antibody is added, the CDR domain remains intact. One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation for producing the claimed invention because humanizing antibodies using human IgG is a conventional technique in the art.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 100, 102, 103, 117, 123 and 129 are rejected under 35 U.S.C. 102(a) as being anticipated by Wu et al. (WO 98/18826) for reasons of record.

Applicant argues that the instant antibodies are distinct from the antibodies of Wu et al. because the PA14 antibody claimed binds to both the N-terminus (Nt) and the second extracellular loop (ECL2) of CCR5 and the antibodies of Wu et al. bind to one or the other.

A review of the reference in view of applicant's arguments has been considered. Contrary to applicant's assertions, Wu et al. specifically anticipate bispecific antibodies that simultaneously bind to Nt and CCL2 of CCR5, see page 15, line 27 to page 16, line 5.

Applicant asserts that antibody 2D7 of Wu et al. binds to a different epitope from PA14 and that the bispecific antibody of Wu et al. recognizes two distinct epitopes whereas the instant PA14 antibody binds to a single epitope that comprises a combination of amino acids in both the Nt and ECL2 regions.

Applicant's arguments have been fully considered, but are found unpersuasive. While the specific antibody 2D7 of Wu et al. binds to Q170 in ECL2, it is noted that PA14 instantly claimed binds to R168 of ECL2 (on page 38, lines 11-15 of the disclosure). The bispecific antibody of Wu et al. anticipates an antibody or a functional portion thereof, "which has the same or similar epitopic specificity as at least two of the antibodies described herein", see page 15,

lines 28-30 of Wu et al. Wu et al. state that the bispecific antibody binds to the Nt and ECL2 and has the same or similar epitopic specificity recognized by mAbs 2D7 and 5C7, see page 15, line 33 to page 16, line 5 (emphasis added). Since the bispecific antibodies of Wu et al. anticipate the same or similar epitopes recognized by 5C7 and 2D7, it is maintained that Wu et al. anticipate a bispecific antibody, or a fragment thereof, that binds to the same epitopes as PA14. PA14 instantly claimed is equivalent to the bispecific antibodies encompassed by Wu et al. as each has bi-specificity (i.e. bispecific) to a combination of two distinct epitopes comprising an amino acid at the Nt and an amino acid within ECL2.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 104, 119, 120, 125, 126, 131 and 132 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wu et al. (WO 98/18826) for reasons of record.

Applicant summarizes the claimed invention and argues that PA14 is not a bispecific antibody and is distinct from the monoclonal antibodies of Wu et al. In view of this, applicant argues that Wu et al. do not teach all of the elements claimed or provide motivation to make the claimed invention with a reasonable expectation of success.

Applicant's arguments have been fully considered, but are found unpersuasive. As stated above, the bispecific antibodies of Wu et al. bind to the same epitopes as instantly claimed antibody PA14. Further, it is maintained that it would have been obvious for one of ordinary

skill in the art at the time the invention was made to obtain the antibody framework from any of the human immunoglobulins to maintain the conformation of the CDR region and to render the recombinant antibodies less immunogenic once administered. Further, one of ordinary skill in the art would have been motivated to maintain the donor amino acid sequences immediately adjacent to the CDR domains to assure that when the framework portion of the antibody is added, the CDR domain remains intact. One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation for producing the claimed invention because humanizing antibodies using human IgG is conventional technique for humanizing recombinant antibodies. Therefore, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made.

***Conclusion***

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Additionally, applicant's submission of an information disclosure statement under 37 CFR 1.97(c) with the fee set forth in 37 CFR 1.17(p) on February 28, 2005 prompted the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a) and § 609(B)(2)(i). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

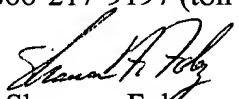
A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37

CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shanon Foley whose telephone number is (571) 272-0898. The examiner can normally be reached on M-F 6:00 AM - 2:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on (571) 272-0902. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Shanon Foley
Primary Examiner
Art Unit 1648